ABSTRACT

Polypeptides comprising all or part of a variant integrin α subunit A domain or a variant integrin β subunit A-like domain are described. In solution or in membrane-associated form, the A domain or the A-like domain of the polypeptides of the invention exists predominantly in a high affinity conformation. In the polypeptides of the invention, referred to as variant integrin polypeptides, a crucial isoleucine residue (described in greater detail below) is absent. The isoleucine can be either deleted or replaced with different amino acids residue, preferably a smaller or less hydrophobic amino acid residue, e.g., alanine or glycine. Because the variant integrin polypeptides of the invention exist in solution or in membrane-associated form predominantly in a high affinity conformation, they are useful in screening assays for the identification of molecules that bind to (and/or mediate the activity of) an integrin. They are also useful for generating antibodies, e.g., monoclonal antibodies, which bind to the high affinity form of an integrin. Some such antibodies recognize an epitope that is either not present or not accessible on an integrin that is in a lower affinity conformation. The variant integrin polypeptides of the invention can be derived from any integrin α subunit or any integrin β subunit and could be used therapeutically. The variant integrin polypeptides preferably include a ligand-binding portion of an A-domain or an A-like domain.